IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

THE MEDICINES COMPANY,	)	
	)	
Plaintiff,	)	
	)	
v.	)	No. 11-cv-1285
	)	
MYLAN INC., MYLAN PHARMACEUTICALS INC., and BIONICHE PHARMA USA, LLC,	)	
	)	
Defendants.	)	

MEMORANDUM OPINION AND ORDER

AMY J. ST. EVE, District Court Judge:

Plaintiff The Medicines Company's ("TMC") has moved to preclude certain opinions of Dr. Ian McKeague offered by Defendant Mylan Inc., Mylan Pharmaceuticals Inc., and Bioniche Pharma USA, LLC (collectively, "Mylan"), pursuant to Federal Rule of Evidence 702 and *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S. Ct. 2786, 125 L. Ed. 2d 469 (1993). For the reasons discussed below, the Court grants in part and denies in part TMC's motion.

BACKGROUND

This action arises out of a patent infringement case involving U.S. Patent No. 7,582,727 (R. 358-1, "the '727 Patent") The '727 patent "relates to a compounding process for preparing a pharmaceutical batch(es) of a drug product or a pharmaceutical formulation(s) comprising bivalirudin as an active ingredient." (*Id.*, '727 patent at col. 2 ll. 29-32) Bivalirudin is the active ingredient in TMC's Angiomax® drug product, an injectable anticoagulant used to prevent blood clotting during coronary procedures. TMC has sold Angiomax® since 2001. Before expiration

of the patents-in-suit, Mylan submitted Abbreviated New Drug Application ("ANDA") No. 202471 to the U.S. Food and Drug Administration ("FDA"), seeking approval to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of a generic equivalent to Angiomax®. TMC claimed that Mylan's ANDA No. 202471 infringes several claims of the patents-in-suit.

On June 21, 2013, Defendant moved for summary judgment of non-infringement or, in the alternative, invalidity, of the '727 patent. (R. 276, Mylan Open Br.) The Court granted in part and denied in part Defendants' motion for summary judgment of non-infringement, invalidity, and willful infringement.[1] (R. 309, Mem, Op, & Order) To support its invalidity theories as to the '727 patent, Mylan disclosed the Expert Report of Ian McKeague, Ph.D. (R. 330-1, McKeague Open Report) In the report, Dr. McKeague opined, in part, that the calculations provided in Table 6 of the '727 patent failed to disclose the true nature of the underlying data. Table 6 lists the mean, standard deviation, and maximum results for certain characteristics of 87 batches of bivalirudin manufactured using "inefficient mixing." (R. 358-1, the '727 patent, col. 22 ll. 10-20.) One of those characteristics is the level of a process impurity known as "Asp9." (*Id*. at col. 22 l. 17.) Table 6 lists a maximum Asp^9 level of 3.6% and a mean of 0.5% with a 0.4% standard deviation for prior art batches made using inefficient mixing. (R. 358-1, the '727 patent, col. 22 ll. 15-25.) The prosecution history provides no additional disclosures related to these values.

Dr. McKeague applied his expertise in statistics to determine what Table 6, from a statistical perspective, conveyed to the Patent Office Examiner concerning the percentage of

[1] The Court granted Defendants' motion for summary judgment of non-infringement of the other patent-in-suit (U.S. Patent No. 7,598,343), and also granted Defendants' motion for summary judgment on Plaintiffs' claim for willful infringement. (R. 309, Mem, Op, & Order)

prior art batches that satisfied the "about 0.6%" Asp^9 maximum recited in the '727 patent claims. (R. 330-4, McKeague Open Expert Report ¶¶ 47-48) In Dr. McKeague's opinion, Table 6 conveyed that approximately 60% of the batches made via inefficient mixing had an Asp^9 value of 0.6% or lower. He then compared this estimation to the actual Asp^9 levels found in these prior art batches and was surprised to learn that 87% had Asp^9 levels at or below 0.6%, and that 90% had Asp^9 levels at or below "about 0.6%." (*Id*. ¶ 48) Based on this, Dr. McKeague concluded that TMC's disclosure in Table 6 "tended to overstate the appearance of difference in the Asp9 results for TMC's 'old' and 'new' compounding processes." (*Id*. ¶ 49)

On April 8, 2013, TMC served the Expert Report of Alan J. Salzberg, Ph.D. in Response to the Expert Report of Ian McKeague, Ph.D. (R. 364-5 Dr. Salzberg Rebuttal Expert Report) In that report, Dr. Salzberg criticized Dr. McKeague's decision to apply a normal distribution to the prior art inefficient mixing data. (*Id*. ¶¶ 9-15) Dr. Salzberg did not dispute the accuracy of Dr. McKeague's calculation based on a normal distribution. Instead, he simply disagreed that it applied. In Dr. Salzberg's opinion, given the low probability that data in Table 6 follows a normal distribution, "conclusions … based solely on a calculation using an assumption of a Normal Distribution are unreliable." (*Id*. ¶¶ 10-11) He did not provide an alternate or better method to calculate the expected Asp^9 levels based on the information provided to the Patent Office.

LEGAL STANDARD FOR *DAUBERT* MOTIONS

"The admissibility of expert testimony is governed by Federal Rule of Evidence 702 and the Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S. Ct. 2786, 125 L. Ed. 2d 469 (1993)." *Lewis v. Citgo Petroleum Corp.*, 561 F.3d 698, 705 (7th Cir. 2009). Rule 702 provides, in relevant part, that "[i]f scientific, technical or other

specialized knowledge will assist the trier of fact[,] . . . a witness qualified as an expert by knowledge, skill, experience, training or education, may testify thereto in the form of an opinion. . . ." *Id.* *See also Happel v. Walmart Stores, Inc.*, 602 F.3d 820, 824 (7th Cir. 2010).

Under the expert-testimony framework, courts perform the gatekeeping function of determining whether the expert testimony is both relevant and reliable prior to its admission at trial. *See id.*; *Power Integrations, Inc. v. Fairchild Semiconductor Intern., Inc.*, 711 F.3d 1348, 1373 (Fed. Cir. 2013); *United States v. Pansier*, 576 F.3d 726, 737 (7th Cir. 2009) ("To determine reliability, the court should consider the proposed expert's full range of experience and training, as well as the methodology used to arrive [at] a particular conclusion."). In doing so, courts "make the following inquiries before admitting expert testimony: first, the expert must be qualified as an expert by knowledge, skill, experience, training, or education; second, the proposed expert must assist the trier of fact in determining a relevant fact at issue in the case; third, the expert's testimony must be based on sufficient facts or data and reliable principles and methods; and fourth, the expert must have reliably applied the principles and methods to the facts of the case." *Lees v. Carthage College*, 714 F.3d 516, 521-22 (7th Cir. 2013); *see also Stollings v. Ryobi Tech., Inc.*, 725 F.3d 753, 765 (7th Cir. 2013); *Power Integrations*, 711 F.3d at 1373; *Pansier*, 576 F.3d at 737.

It is clear that "genuine expertise may be based on experience or training." *United States v. Conn*, 297 F.3d 548, 556 (7th Cir. 2002) (quoting *Tyus v. Urban Search Mgmt.*, 102 F.3d 256, 263 (7th Cir. 1996)). "[W]hile extensive academic and practical expertise in an area is certainly sufficient to qualify a potential witness as an expert, Rule 702 specifically contemplates the admission of testimony by experts whose knowledge is based on experience." *Trustees of Chicago Painters & Decorators Pension, Health & Welfare, & Deferred Sav. Plan Tr. Funds v.*

Royal Int'l Drywall & Decorating, Inc., 493 F.3d 782, 787-88 (7th Cir. 2007) (citations and quotations omitted). As such, courts "consider a proposed expert's full range of practical experience, as well as academic or technical training, when determining whether that expert is qualified to render an opinion in a given area." *Id.* (quoting *Smith v. Ford Motor Co.*, 215 F.3d 713, 718 (7th Cir. 2000)).

Finally, it is important to bear in mind the Seventh Circuit's teaching about the critical distinction between a jury trial and a bench trial with respect to the Rule 702 inquiry:

> Where the gatekeeper and the factfinder are one and the same – that is, the judge – the need to make such decisions prior to hearing testimony is lessened. *See United States v. Brown*, 415 F.3d 1257, 1268-69 (11th Cir. 2005). That is not to say that the scientific reliability requirement is lessened in such situations; the point is only that the court can hear the evidence and make its reliability determination during, rather than in advance of, trial. Thus, where the factfinder and the gatekeeper are the same, the court does not err in admitting the evidence subject to the ability later to exclude it or disregard it if it turns out not to meet the standard of reliability established by Rule 702.

In re Salem, 465 F.3d 767, 777 (7th Cir. 2006); *see also Metavante Corp. v. Emigrant Sav. Bank*, 619 F.3d 748, 760 (7th Cir. 2010) (observing that "the court in a bench trial need not make reliability determinations before evidence is presented" because "the usual concerns of the rule – keeping unreliable expert testimony from the jury – are not present in such a setting"); *Brown*, 415 F.3d at 1269 ("There is less need for the gatekeeper to keep the gate when the gatekeeper is keeping the gate only for himself."). Under this sensible approach, where there is no jury and the judge will serve as the trier of fact at trial, the Court may choose to (1) allow the presentation of borderline testimony, (2) subject the testimony to the rigors of cross-examination, and (3) decide later whether the testimony is entitled to some consideration or whether it should be excluded as irrelevant, unreliable, or both.

ANALYSIS

TMC seeks to exclude certain opinions of Dr. Ian McKeague. First, TMC asks the Court to preclude Dr. McKeague's "Normal Distribution" statistical analysis of Table 6 because it is "unreliable." Second, TMC seeks to preclude Mylan's experts Dr. Nancy J. Linck and Dr. David E. Auslander from testifying in reliance on Dr. McKeague's "unreliable" Table 6 analysis.[2] Third, TMC seeks to preclude Dr. McKeague's opinions regarding what the Patent Office Examiner would have done or thought because such opinions constitute irrelevant speculation. The Court will address each argument in turn.

I. Dr. McKeague

TMC does not challenge Dr. McKeague's qualifications to testify as an expert in this case, but the Court nevertheless summarizes them. Dr. McKeague is a Professor of Biostatistics at Columbia University. He received a Ph.D. at the University of North Carolina at Chapel Hill in 1980. He then took a position as an Assistant Professor in the Department of Statistics at Florida State University, where he became a full Professor in 1991. Dr. McKeague has received numerous professional acclaims, including serving as a Fellow of the Institute of Mathematical Studies and a Fellow of the American Statistical Association.

Dr. McKeague's research focuses on functional data analysis, empirical likelihood, and non-standard asymptotics. He is the named author in 88 peer-reviewed articles and has received grants from a number of organizations including the National Institutes of Health ("NIH") and the National Science Foundation ("NSF"). In addition to teaching and research, Dr. McKeague has worked as a consultant on clinical trials and statistical analysis for nearly twenty years.

[2] TMC has moved to preclude Dr. Linck's and Dr. Auslander's opinions on other grounds, in two other *Daubert* motions, which the Court will address separately.

In his expert report, Dr. McKeague provided a statistical analysis regarding Asp^9-bivalirudin impurity data in Table 6 of the '727 patent. (R. 330-1, McKeague Open Report) Specifically, Dr. McKeague applied a normal distribution to the data in Table 6, which led him to a statistical estimate "that 60% of bivalirudin made using TMC's pre-2006 process had an ASP9 level of 0.6% or lower." (*Id*. ¶¶ 47-49) He then compared this estimation to the actual Asp^9 levels found in these prior art batches and was surprised to learn that 87% had Asp^9 levels at or below 0.6%, and that 90% had Asp^9 levels at or below "about 0.6%." (*Id*. ¶ 48) Based on this, Dr. McKeague concluded that TMC's disclosure in Table 6 "tended to overstate the appearance of difference in the Asp9 results for TMC's 'old' and 'new' compounding processes." (*Id*. ¶ 49)

II. Dr. McKeague's "Normal Distribution" Analysis is Not Unreliable

TMC first moves to preclude Dr. McKeague's normal distribution analysis as "unreliable" concerning Asp^9-bivalirudin impurity data in Table 6 of the '727 patent. (R. 327 at 4) TMC alleges that Dr. McKeague's conclusions based on his analysis of Table 6 are unreliable, and therefore inadmissible, because "[t]he Asp9 values in Original Angiomax® do not follow a 'normal distribution,'" (R. 327 at 3) Further, TMC's expert, Dr. Alan J. Salzberg, claims there is a low probability that the Asp^9 values follow a normal distribution, but fails to suggest any alternate distribution to analyze the data.

According to Dr. McKeague, the most conservative statistical analysis approach for a "reasonable statistician" to apply to a set of data is a "normal distribution," given the information provided in Table 6, which provides impurity data (mean, standard deviation, and maximum) for 87 Original Angiomax® batches. (R. 330-4, McKeague Second Reply at 4). TMC argues that Dr. McKeague "appeared to disavow the assumption [of a normal distribution] underlying his

opinions in his expert report" based on his deposition testimony that he was "not assuming a normal distribution" but was instead, in his report, basing his opinions on the hypothetical "if you assume a normal distribution . . . ." (R. 327 at 4-5.) TMC takes this quote out of context as Dr. McKeague merely clarified that he was not offering an opinion as to whether the undisclosed underlying data followed a normal distribution.[3] Dr. McKeague again explained that a "reasonable statistician" would assume a normal distribution in such circumstances. (R. 330-5, McKeague Dep. at 159:24-160:17) ("The reasonable statistician would use a normal distribution."). TMC does not contest that the normal distribution analysis is a well-known statistical methodology, or that the analysis is inherently unreliable or flawed. TMC's expert Dr. Alan Salzberg merely asserts that the normal distribution method likely does not apply to the information in Table 6.

The Court finds TMC's "unreliability" arguments unavailing. Dr. Salzberg's disagreement does not transform Dr. McKeague's use of an accepted method into an unreliable methodology. "An expert may provide expert testimony based on a valid and properly applied methodology and still offer a conclusion that is subject to doubt." *Stollings*, 725 F.3d at 766. Here, Dr. McKeague based his conclusions regarding Asp^9 impurity data on a valid methodology, the "normal distribution" analysis, and consistently maintained his position that a "reasonable statistician" would do the same, when presented with the same information. While TMC challenges Dr. McKeague's choice of methodology and doubts his ultimate conclusions, these arguments go to the weight of the expert testimony, not its admissibility. *See Stollings*, 725 F.3d at 765 (7th Cir. 2013) ("The soundness of the factual underpinnings of the expert's analysis and

[3] Dr. McKeague stated: "Without having any information about the distribution, I can't come up with a number. So I assume a normal distribution and I come up with a number." (R. 330-5, McKeague Dep at 158:2-11)

the correctness of the expert's conclusions based on that analysis are factual matters to be determined by the trier of fact." (quoting *Ford Motor Co.*, 215 F.3d at 718). Additionally, when experts merely disagree about the application of a well-known methodology, the Court may weigh the expert's testimony at trial, not exclude it. *Civix v. Expedia*, 03 C 03792, 2005 WL 5961023, at *3 (N.D. Ill. Oct. 25, 2005).[4] While TMC and its expert Dr. Salzberg certainly disagree with Dr. McKeague's conclusions and the methodology he chose to reach them, it can address these issues through rigorous cross-examination at trial if it so chooses. *Stollings*, 725 F.3d at 766; *Lapsley v. Xtek, Inc.*, 689 F.3d 802, 805, 810-11, 817 (7th Cir. 2012). TMC's unreliability argument against conclusions reached by Dr. McKeague on the basis of a normal distribution analysis of Table 6 fails.

III. Mylan's Other Experts May Rely on Dr. McKeague's Analysis

TMC further contends that the Court should preclude Mylan experts Nancy J. Linck and Dr. David E. Auslander from testifying in reliance on Dr. McKeague's Table 6 statistical analysis and conclusions. Expert testimony need not be based on first-hand knowledge or research actually conducted by the expert himself. *See Daubert*, 509 U.S. at 592; *Walker v. Soo Line R.R.*, 208 F.3d 581, 588 (7th Cir. 2000) ("Indeed, courts frequently have pointed to an expert's reliance on the reports of others as an indication that their testimony is reliable."). Here, as explained above, Dr. McKeague, a qualified statistical expert, employed a reliable method to analyze the data in Table 6. Thus, Dr. Linck and Dr. Auslander certainly can rely on testimony

[4] *See also Cook v. Rockwell Int'l Corp.*, 580 F. Supp. 2d 1071, 1092 (D. Colo. 2006) ("This is a classic disagreement between experts that goes to the credibility of each expert's opinions, not to the reliability of their methodology within the meaning of Rule 702."); Weinstein's Federal Evidence § 702.05 ("Experts often disagree. A trial court's determination that the proffered testimony of one expert witness is reliable and helpful does not necessarily mean that the contradictory testimony of another witness, concerning the same subject matter but using a different methodology, is not also reliable and helpful.").

and reports from Dr. McKeague's analysis of Table 6 in formulating their own, expert opinions. TMC's motion on this issue is denied.

IV. Dr. McKeague's Opinions Regarding the Significance of the Asp[9] Levels of Prior Art Batches are Admissible

TMC also moves to exclude two statements by Dr. McKeague regarding "what the Patent Office Examiner would have concluded based on the table [Table 6] and what additional information the examiner would have found material." (R. 327 at 8-11) Specifically, TMC alleges these two statements made by Dr. McKeague are "speculative testimony" relating to "what the Patent Office Examiner would have concluded" or believed to be "material." (R. 399, TMC's R. Br. at 5)

First, Dr. McKeague may provide factual context to support Mylan's theories of inequitable conduct, but he may not speculate as to "what the Patent Office Examiner would have concluded."[5] *See, e.g., Se-Kure Controls, Inc. v. Diam USA, Inc.*, No. 06 C 4857, 2009 WL 77463, at *2 (N.D. Ill. Jan. 9, 2009) (curtailing the expert's proposed testimony and explaining that experts are not "mind-reader[s]"); *Applied Materials, Inc. v. Advanced Semiconductor Materials Am., Inc.*, No. C 92-20643, 1995 WL 261407, at *2 (N.D. Cal. Apr. 25, 1995) ("The court grants Applied's motion precluding Nusbaum from testifying about what the examiner would have done if Nusbaum had been the examiner, or if the examiner had different information. The evidence would be irrelevant speculation . . . .").

[5] Dr. McKeague stated: ". . . looking at the information in Table 6, the Examiner reasonably would have concluded that the prior art Angiomax did not "consistently" achieve an Asp9 level at or below about 0.6%." (R. 330-2, McKeague Reply Report ¶ 14) (emphasis added)

Second, on the issue of materiality[6] of the data, Dr. McKeague's education and experience make him more than qualified to review and assess the data in Table 6 as a statistician, and to provide his opinion, without testifying as to matters of law. *See Bone Care Int'l. LLC v. Pentech Pharms., Inc.*, No. 08 C 1083, 2010 WL 3928598, at *15 (N.D. Ill. Oct. 1, 2010) ("[Expert] may provide factual context that goes to the underlying contentions of inequitable conduct, obviousness, priority, and other key legal issues, but he may not speculate or offer his subjective conclusions on those contentions.").

TMC also argues that Dr. McKeague cannot provide materiality opinions because he is not a chemist. (R. 327 at 11) McKeague's opinions regarding materiality, however, are confined to his field of expertise, statistics. Experts are permitted to opine on materiality and make relevant testimony even in fields beyond their expertise. *CBOE v. ISE*, No. 07 C 623, ECF No. 701 at 3-4 (N.D. Ill. March 7, 2013) (citing *Sundance, Inc. v. DeMonte Fabricating Ltd.*, 550 F.3d 1356, 1363 n.5 (Fed. Cir. 2008)) (allowing relevant expert testimony from expert who did not have "ordinary skill in the field of computer programming," the relevant art). Furthermore, the relevance of McKeague's statistical opinions on materiality is further supported by TMC co-inventor Dr. Gopa Krishna, a chemist, who testified that a full understanding of the Asp[9] limitation recited in the '727 patent requires statistical analysis. Greb Opp'n Decl. Ex. 8 (Del. Krishna Tr.) at 555:18-22 ("that is a . . . statistical reviewer's question"), 746:16-23 ("it's a statistical issue and I'm not a statistician"); Greb Opp'n Decl. Ex. 9 (Krishna Tr.) at 215: 23-25 ("I don't know . . . [i]t is more like a statistical answer.").

[6] Information is "material" when "the PTO would not have allowed a claim had it been aware of the undisclosed prior art." *Am. Calcar, Inc. v. Am. Honda Motor Co., Inc.*, 651 F.3d 1318, 1334 (Fed. Cir. 2011)

With those caveats in mind, the Court denies Plaintiff's motion to preclude Dr. McKeague from testifying as to factual matters relating to his expertise in statistics and their potential materiality in the patent application process, but grants Plaintiff's motion to preclude Dr. McKeague from opining on what the Patent Office Examiner would have done or thought in light of Dr. McKeague's statistical analysis.

CONCLUSION

For the reasons discussed in detail above, the Court denies TMC's motion to preclude Dr. McKeague's conclusions stemming from his "Normal Distribution" statistical analysis of Table 6, denies TMC's motion to preclude Mylan's experts Nancy J. Linck and Dr. David E. Auslander from testifying in reliance on Dr. McKeague's conclusions, and grants in part TMC's motion to preclude Dr. McKeague's opinions regarding what the Patent Office Examiner would have done or thought, but denies TMC's motion to preclude Dr. McKeague's testimony relating to the materiality of his conclusions.

Dated: March 27, 2014

AMY J. ST. EVE
United States District Court Judge